AMENDMENTS TO THE SPECIFICATION

IN THE SPECIFICATION

On page 3, line 27, please replace the original paragraph with the following amended paragraph:

-- In the context of the present invention the term "functional fragment or derivative" refers to amino acid sequences which differ from the amino acid sequence of SEQ ID NO:1 in one or more positions and share a high degree of homology to that sequence. Homology means thereby a sequence identity over the overall length of at least 70%, preferably 80%, more preferably 90%. The deviations to SEQ ID NO:1 can originate from deletions, additions, substitutions or insertions. A fragment or derivative is considered "functional", when it is capable of binding to sulphate and/or phosphate groups. One possible test for functionality is provided in the example section (see Methods: "Turbidometric aggregation assays"). Furthermore, "fragment" refers to a peptide of 5, 6, 7, 8, 9, 10, 11, up to 20 amino acids or to a protein of at least 20, 25, 50, 100, or more amino acids. Typically, a fragment comprises at least 8, 10, 12, 14, 16 or more contiguous amino acids of the amino acid sequence of SEQ ID NO:1. Particularly, the polypeptide refers to a sequence comprising the amino acids GRVEVLYRGSW **(SEQ ID NO: 9)** which is present several times within SEQ ID NO:1, and multiples thereof, and which represents the 11 amino acid motif that binds sulfate and phosphate groups.--

On page 4, line 7, please replace the original paragraph with the following amended paragraph:

-- Furthermore, the polypeptide refers to a sequence comprising the amino acids GRVEILYRGSW **(SEQ ID NO: 10)** and/or GRVEVLYQGSW **(SEQ ID NO: 11)**.--

On page 20, line 20, please replace the original paragraph with the following amended paragraph:

-- **Fig. 1** Definition of the DMBT1 pathogen-binding site. *a*, Domain structure of the DMBT1-variant presumably expressed from the largest (wild type) *DMBT1* allele (*DMBT1*^{wt}) with the position of the synthetic peptides in the consensus sequence **(SEQ ID NO: 12)** of the 13 amino-

terminal SRCR domains depicted below. Peptides in red mediated aggregation and peptides marked with asterisks exerted activity in binding of Gram-positive *S. mutans* and Gram-negative *E. coli* bacteria. The 11 amino acid stretch marked in red in the SRCR consensus is the minimal pathogen-binding site (DMBT1pbs1) predicted from these assays. Pink triangle: leader peptide; blue box: DMBT1-specific motif; red ovals: SRCR domains; orange ovals: SRCR interspersed domains (SIDs); purple boxes: C1r/C1s-Uegf-Bmp1 (CUB) domains; green oval: *zona pellucida* (ZP) domain; EHD: ebnerin-homologous domain. ***b***, The results from binding analyses with *S. mutans* are shown. Colour and alphabetical codes correspond to these in Fig. 1*a*. Error bars are SEM. ***c***, Confirmation of the minimal binding site DMBT1pbs1. The top panel summarizes the results of binding (B) and aggregation (A) studies with DMBT1pbs1 and amino- and carboxy-terminally truncated variants of the peptide sequence. (+) binding and aggregation activity; (-) no binding and no aggregation activity. The graphs below display the aggregation of Gram-positive *S. gordonii* (purple) and *S. mutans* (red) and of Gram-negative *H. pylori* (dark blue) and *E. coli* (light blue) in the presence (top graph) and absence (bottom graph) of the DMBT1pbs1-peptide. ***d***, Analysis of critical amino acid residues and corresponding motifs in related proteins. The graph at the left displays the impact of amino acid substitution by alanine of the residues depicted on the right. Binding activity to *S. mutans* is expressed as percent compared to DMBT1pbs1, which served as positive control (PC). SRCRP1 without substantial binding activity was included as negative control (NC). Error bars are SEM. Amino acid residues critical for binding are marked in orange. The right panel summarizes the results from DMBT1pbs1-corresponding motifs in other SRCR proteins. (B) and (A) denote group B and group A SRCR proteins. (+) bacterial binding and aggregation activity and (-) no bacterial binding and aggregation activity with both Gram-positive *S. mutans* and Gram-negative *E. coli*. Amino acids diverging from DMBT1pbs1 are marked in blue. Boxed residues are compatible substitutions. h: human; r: rabbit; c: cattle; m: mouse. Note that sequence variations present in the 13 amino-terminal domains of human DMBT1 and in its orthologs in other species are allowed. The motif present in SRCR14 of DMBT1 and, for example, the corresponding motifs of the Mac-2bp and MARCO did not exert binding or aggregation activity. ***e***, Quantitative and qualitative differences between the DMBT1pbs1-motifs present in the SRCR domains of DMBT1. Motifs present in SRCR1, SRCR2-7, SRCR9-11, and SRCR13 exerted best binding and aggregation activity (results shown for *S. mutans*). While the motif present in SRCR8 and SRCR12 was less active, the motif in the carboxy-terminal SRCR14 exerted no activity at all.--

On page 24, line 4, please replace the original paragraph with the following amended paragraph:

-- **Fig. 6** Generation of *Dmbt1*$^{-/-}$ mice. ***a***, Schematic presentation of the domain organization of mouse Dmbt1 (top line). The pink triangle represents the leader peptide. The pink box below denotes the part of the leader peptide encoded by exon 1 with the genomic **(SEQ ID NO: 13)** (bold letters: exonic sequence; normal letters: intronic sequence) and the amino acid sequence **(SEQ ID NO: 14)** depicted below. Blue box: small sequence without homology encoded by exon 2; SRCR: scavenger receptor cysteine-rich domain; CUB: C1r/C1s-Uegf-Bmp1 domain; ZP: *zona pellucida* domain; EHD: Ebnerin-homologous domain. Orange ovals indicate SRCR interspersed domains (SIDs); TTT and STP are threonine and serine-threonine-proline-rich domains, respectively. Following lines: schematical presentation of the wild type allele as contained in genomic subclone *Dmbt1*c1, the targeting construct, and the knockout allele after Cre-mediated recombination. Red box: targeted 1224-bp region containing exon 1 (pink box) as well as about 900 bp of the promoter region; blue box: exon 2; yellow boxes: selection cassettes; yellow triangles: LoxP sites; gray boxes: probes used for the identification of ES-cells with homologous recombination (*Dmbt1*/KOa) and for the identification of ES cells and mice carrying the knockout allele (*Dmbt1*/KOb). ***b***, Southern blot analysis of mouse genomic DNA with probe *Dmbt1*/KOb demonstrated the wild type 4.1-kb *Bgl*II fragment in *Dmbt1*$^{+/+}$ mice, while *Dmbt1*$^{-/-}$ displayed the deleted 2.9-kb *Bgl*II fragment, and *Dmbt1*$^{+/-}$ mice were heterozygous for the two alleles. ***c***, Northern blot analysis of small intestine RNA with probe *DMBT1*/8kb-3.8 (top panel) and a ß-actin probe (bottom panel). The expected size of the *Dmbt1* transcript is 6.6 kb. ***d***, Western blot analysis of protein extracts from mouse small intestines with polyclonal anti-DMBT1^{GP340} (upper panel) and anti-DMBT1^{SAG} (lower panel). Arrowheads mark the position of the 210-kDa marker band. ***e***, RNA *in situ* hybridization and ***f***, immunohistochemical analysis (anti-DMBT1^{SAG}) of distal duodenum sections of *Dmbt1*$^{+/+}$ and *Dmbt1*$^{-/-}$ mice.--

On page 28, line 7, please replace the original paragraph with the following amended paragraph:

-- Initially, it was intended to refine in more detail the bacterial binding site of DMBT1, which we previously mapped to a 16 amino acid motif (designated as SRCRP2) present in most of its scavenger receptor cysteine-rich (SRCR) domains. We identified a minimal sequence of 11 amino acids (GRVEVLYRGSW **(SEQ ID NO: 9)**; DMBT1 pathogen-binding site 1; DMBT1pbs1) to be sufficient and necessary for interaction with Gram-positive and -negative bacteria (Fig. 1*a-c*). Corresponding motifs present in the 13 amino-terminal SRCR domains of DMBT1 and in its orthologs in other species (mouse, rat, rabbit, cattle) likewise exerted bacterial binding activity, but not these in SRCR14 of human DMBT1 or in other SRCR proteins (Fig. 1*d, e*). This strongly suggests functional equivalence of

DMBT1 and its orthologs, while its fourteenth SRCR domain probably is functionally distinct. Besides DMBT1, only the group A SRCR proteins SR-A and MARCO, which are cell surface receptors on immune cells, is demonstrated to interact with bacteria. While the positively charged RXR motif mediates binding of MARCO to polyanionic substances by electrostatic interactions, we identified the negatively charged motif VEVL **(SEQ ID NO: 15)** and a terminal tryptophan residue as critical for DMBT1pbs1 (Fig. 1*d*), pointing to a distinct mode of pathogen-recognition.--

On page 43, line 13, please replace the original paragraph with the following amended paragraph:

-- Starting from a 10-kb *Hind*III mouse genomic fragment subcloned into pBluescript SK(-) (*Dmbt1*c1; Fig. 1*a*), a 4.1-kb *Pst*I/*Hinc*II fragment was cloned 5` to a LoxP site utilizing the preceding *Hind*III recognition site to give rise to the left homology arm. The 1224-bp *Hinc*II/*Aci*I fragment was amplified from *Dmbt1*c1 using primers introducing a 5` *Spe*I and a 3` *Xba*I site (*Dmbt1*/KOcf1: 5`-GCA CTA GTG GCA AGG TAA AGG AGG CAA G-3`**(SEQ ID NO: 3)**; *Dmbt1*/KOcr1: 5`-TGT CTA GAC CTT CAC CGA ACG ACT CC-3`) **(SEQ ID NO: 4)** and subsequently inserted 3` to the LoxP site. A 4.0-kb *Aci*I/*BamH*I fragment (the latter site locating within the vector sequence) from *Dmbt1*c1 was separately subcloned 3` to a NeoTK cassette flanked by two LoxP sites to give rise to the right homology arm. The insert was then excised and cloned 3` to the *Hinc*II/*Aci*I fragment. A diphtheria toxin A (DTA) cassette under the control of the MCI promoter allowing for negative selection of non-homologous recombinants was cloned 5` to the left homology arm to give rise to the final targeting construct (Fig. 1*a*).--

On page 43, line 28, please replace the original paragraph with the following amended paragraph:

-- Twenty-five µg linearized plasmid DNA of the targeting construct was transfected into 1 x 10^7 E14.1 mouse ES-cells by electroporation using standard conditions. Southern blot screens of 240 G418-resistant ES-cell clones using probe *Dmbt1*/KOa (340-bp PCR product amplified with primers *Dmbt1*/KOaf1: 5`-CCC AGT GTC AGT GAG CTT AG-3` **(SEQ ID NO: 5)** and *Dmbt1*/KOar1: 5`-GCT CAA CAA CTG CTA CCA TAC-3`**(SEQ ID NO: 6)**; Fig. 1*a*), yielded 3 clones heterozygous for the new 4.7-kb *Hind*III fragment representing the targeted allele. Single integration into the authentic site was further confirmed by hybridization with a Neo probe. Transient transfection of 3 x 10^6 cells of ES cell clone 2 with 5 µg Cre-recombinase encoding plasmid DNA and Southern blot analysis (probe: *Dmbt1*/KOb; Fig. 1*a*) of 126 subclones delivered 13 clones heterozygous for the 2.9-kb *Bgl*II fragment representing the knockout allele (Fig. 1*a*). Sixty-nine C57BL/6 blastocyst

injections and embryo-transfer to pseudopregnant foster mothers yielded 10 highly chimaeric males (> 90% coat chimaerism). Three of four males mated with C57BL/6 females displayed germline transmission of the knockout allele. By intercrosses of heterozygous F1 mice we obtained homozygous mutant F2 *Dmbt1*$^{-/-}$ mice at expected Mendelian frequencies. Mouse tail biopsies were used for genotyping with probe *Dmbt1*/KOb (480-bp PCR product amplified with primers *Dmbt1*/KObf1: 5`- CTT TTG TGG GGT CAA ATT CTG TC-3` **(SEQ ID NO: 7)**and *Dmbt1*/KObr1: 5`-CTG TTG GTC CCT TGA CCT G-3` **(SEQ ID NO: 8)**) by Southern blotting as shown in Fig. 1*b*.--

On page 48, line 1, please replace the original paragraph with the following amended paragraph:

-- **Synthetic peptides.** The synthetic peptide DMBT1-SRCRP2 (NH_2-QGRVEVLYRGSWGTVC-COOH **(SEQ ID NO: 16)**; purity >85%) comprising the pathogen-binding site of DMBT1 was obtained from Eurogentec (Belgium) and resuspended to a final concentration of 1 mg/ml in $H_2O_{bidest.}$ containing 10% v/v DMSO.--